

Amendments to the Claims:

Claims 1, 3-12, 15-19, 21, 39, 40 and 42-55 are pending.

Please cancel claim 19.

Please amend claims 1, 3, 18, 39, 42, 43, 47 and 50 as shown below.

Please add claims 56-101 as shown below.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for separating a polynucleotide molecule from a population of nucleic acid molecules, the method comprising;

(a) providing a population of nucleic acid molecules comprising said polynucleotide molecule, wherein

(i) said population of nucleic acid molecules is comprises genomic DNA or RNA molecules, and

(ii) one strand of said polynucleotide molecule includes comprises a first target nucleic acid sequence and a first distinguishing element,

(iii) said first target nucleic acid sequence is within 100 nucleotides of said a first distinguishing element in said one strand of said polynucleotide molecule, and

(iv) said distinguishing element distinguishes said polynucleotide molecule from a genomic DNA or RNA molecule that is nearly identical to said polynucleotide molecule;

(b) contacting said population of nucleic acid molecules with a first targeting element, wherein said first targeting element binds specifically to said first target nucleic acid sequence of said polynucleotide molecule;

(c) selectively and covalently attaching a first separation group to said bound first targeting element, wherein attachment of said first separation group occurs only if said first

targeting element is bound to said first target nucleic acid sequence and said first distinguishing element is within 100 nucleotides of the location to which said bound first targeting element binds;

(d) immobilizing said polynucleotide and said bound first targeting element via said attached first separation group to a substrate, thereby forming an immobilized first targeting element-separation group complex comprising the polynucleotide molecule of step (a); and

(e) removing said immobilized first targeting element-separation group complex comprising said polynucleotide molecule of step (a) from said population of nucleic acid molecules, wherein said polynucleotide molecule remains bound to said immobilized targeting element-separation group following said removal, thereby separating said polynucleotide molecule of step (a) from said population of nucleic acid molecules.

2. (Canceled)

3. (Currently Amended) The method of claim 1, wherein said ~~first targeting element binds to said polynucleotide molecule at a first target nucleic acid sequence~~ is within 20 nucleotides of said first distinguishing element in said one strand of said polynucleotide molecule.

4. (Previously Presented) The method of claim 1, wherein said first targeting element comprises a nucleic acid sequence.

5. (Previously Presented) The method of claim 4, wherein said first targeting element is an oligonucleotide.

6. (Original) The method of claim 5, wherein said oligonucleotide has an extendable 3' hydroxy terminus.

7. (Previously Presented) The method of claim 6, wherein said first separation group is an immobilizable nucleotide.

8. (Original) The method of claim 7, wherein said immobilizable nucleotide is a biotinylated nucleotide.

9. (Previously Presented) The method of claim 8, wherein said first separation group is attached to said first targeting element by extending said oligonucleotide with a polymerase in the presence of said biotinylated nucleotide, thereby forming an extended oligonucleotide primer containing said immobilizable nucleotide.

10. (Previously Presented) The method of claim 3, wherein said first targeting element is an oligonucleotide.

11. (Previously amended) The method of claim 10, wherein said first separation group is an immobilizable nucleotide.

12. (Original) The method of claim 11, wherein said immobilizable nucleotide is a biotinylated nucleotide.

13. (Canceled)

14. (Canceled)

15. (Original) The method of claim 1, wherein said population of nucleic acid molecules is a population of RNA molecules.

16. (Previously Presented) The method of claim 1, wherein said first distinguishing element is a single nucleotide polymorphism.

17. (Previously Presented) The method of claim 1, wherein said substrate is a particle, bead, magnetic bead, or glass surface.

18. (Currently Amended) The method of claim 1, further comprising contacting said population of nucleic acid molecules with a second targeting element simultaneously with said first targeting element, wherein

(i) said second targeting element binds specifically to a second target nucleic acid sequence in one strand of a second polynucleotide molecule in said population of nucleic acid molecules,

(ii) wherein said one strand of said second polynucleotide molecule further comprises a second distinguishing element,

(iii) said second target nucleic acid sequence is located within 100 nucleotides of a said second distinguishing element in said one strand of said polynucleotide molecule, in said population of nucleic acid molecules and

(iv) said second distinguishing element distinguishes the second polynucleotide molecule from a second genomic DNA or RNA molecule that is nearly identical to the second polynucleotide molecule;

attaching a second separation group to said second bound targeting element;

immobilizing said attached second targeting element via said attached second separation group to a substrate, thereby forming a second immobilized targeting element-separation group complex comprising said second polynucleotide molecule; and

removing said immobilized second targeting element-separation group complex comprising said second polynucleotide molecule from said population of nucleic acid molecules, thereby separating said second polynucleotide molecule from said population of nucleic acid molecules.

19. (Canceled)

20. (Canceled)

21. (Previously Presented) The method of claim 1 wherein said population of DNA molecules is a population of genomic DNA molecules.

22. – 38. (Canceled)

39. (Currently Amended) A method for separating a polynucleotide molecule from a population of nucleic acid molecules, the method comprising:

(a) providing a population of nucleic acid molecules comprising at least one polynucleotide molecule, wherein

(i) said population of nucleic acid molecules is comprises genomic DNA or RNA molecules, and wherein

(ii) one strand of said polynucleotide molecule includes comprises a target nucleic acid sequence and a distinguishing element,

(iii) said target nucleic acid sequence is within 100 nucleotides of said a distinguishing element in said one strand of said polynucleotide molecule, and

(iv) said distinguishing element distinguishes said polynucleotide molecule from a genomic DNA or RNA molecule that is nearly identical to said polynucleotide molecule;

(b) contacting said population of nucleic acid molecules with an oligonucleotide that binds specifically to said target nucleic acid sequence of said polynucleotide molecule;

(c) selectively and covalently attaching a separation group to said bound oligonucleotide, wherein said separation group comprises an immobilizable nucleotide, and wherein attachment of said separation group occurs only if said oligonucleotide is bound to said target nucleic acid sequence and said first distinguishing element is within 100 nucleotides of the location to which said bound first targeting element binds;

(d) immobilizing said bound oligonucleotide via said immobilizable nucleotide of said attached separation group to a substrate, thereby forming an immobilized oligonucleotide-separation group complex; and

(e) removing said immobilized oligonucleotide-separation group complex from said population of nucleic acid molecules, wherein said polynucleotide molecule remains bound to said immobilized oligonucleotide-separation group following said removal, thereby separating said polynucleotide molecule of step (a) from said population of nucleic acid molecules.

40. (Previously Presented) The method of claim 39, wherein said oligonucleotide has an extendable 3' hydroxy terminus.

41. (Canceled)

42. (Currently Amended) The method of claim 39, wherein said immobilizable nucleotide is a biotinylated nucleotide, and said separation group is attached to said oligonucleotide by extending said oligonucleotide with a polymerase in the presence of said biotinylated nucleotide, thereby forming an extended oligonucleotide primer containing said immobilizable nucleotide.

43. (Currently Amended) A method for separating a nucleic acid sequence of interest from a population of nucleic acid molecules, the method comprising;

providing a population of nucleic acid molecules comprising a nucleic acid sequence of interest, wherein one strand of said nucleic acid sequence of interest comprises includes a target nucleic acid sequence and a single nucleotide polymorphism, and wherein said target nucleic acid sequence is within 100 nucleotides of said a single nucleotide polymorphism in said one strand of said nucleic acid sequence of interest;

contacting said population of nucleic acid molecules with a targeting element, wherein said targeting element binds specifically to said target nucleic acid sequence of said nucleic acid sequence of interest;

selectively and covalently attaching a separation group to said bound targeting element, wherein attachment of said separation group occurs only if said single nucleotide

polymorphism is within 100 nucleotides of the location to which said bound targeting element binds;

immobilizing said bound targeting element via said attached separation group to a substrate, thereby forming an immobilized targeting element-separation group complex comprising said nucleic acid sequence of interest; and

removing said immobilized targeting element-separation group complex comprising said nucleic acid sequence of interest from said population of nucleic acid molecules, thereby separating said nucleic acid sequence of interest from said population of nucleic acid molecules.

44. (Previously Presented) The method of claim 43, wherein said nucleic acid sequence of interest is an amplified nucleic acid sequence.

45. (Previously Presented) The method of claim 43, wherein the covalent attachment of a separation group occurs through ligation.

46. (Previously Presented) The method of claim 43, wherein the covalent attachment of a separation group occurs by extending an oligonucleotide with a polymerase.

47. (Currently Amended) A method for separating a ~~fragment of~~ genomic DNA fragments from a population of nucleic acid molecules, the method comprising;

(a) providing a population of nucleic acid molecules comprising a first ~~fragment of genomic DNA fragment~~, wherein

(i) one strand of said first fragment of genomic DNA fragment ~~includes-comprises~~ a target nucleic acid sequence and a distinguishing element,

(ii) said target nucleic acid sequence is -within 100 nucleotides of said a-distinguishing element in said one strand of said first genomic DNA fragment, and

(iii) said distinguishing element distinguishes said first genomic DNA fragment from a second genomic DNA fragment that is nearly identical to said first genomic DNA fragment;

(b) contacting said population of nucleic acid molecules with an oligonucleotide probe that binds specifically to said target nucleic acid sequence in ~~said fragment of first genomic DNA fragment~~;

(c) selectively and covalently attaching a separation group to said bound oligonucleotide probe, wherein said separation group is an immobilizable nucleotide and attachment occurs only if said oligonucleotide probe is bound to said target nucleic acid sequence and said distinguishing element is present within 100 nucleotides of the location to which said bound oligonucleotide probe binds;

(d) immobilizing said bound oligonucleotide probe via said immobilizable nucleotide of said attached separation group to a substrate, thereby forming an immobilized oligonucleotide probe-separation group complex comprising the fragment of genomic DNA of step (a); and

(e) removing said immobilized oligonucleotide probe-separation group complex comprising ~~the fragment of said first genomic DNA fragment~~ of step (a) from said population of nucleic acid molecules, wherein said target nucleic acid sequence remains bound to said immobilized oligonucleotide probe-separation group following said removal, thereby separating said ~~first fragment of genomic DNA fragment~~ from said population of nucleic acid molecules.

48. (Previously Presented) The method of claim 47, where the distinguishing element is a polymorphism.

49. (Previously Presented) The method of claim 47, wherein the polymorphism is a single nucleotide polymorphism.

50. (Currently Amended) A method for separating a polynucleotide molecule from a population of nucleic acid molecules, the method comprising;

(a) providing a population of nucleic acid molecules comprising said polynucleotide molecule, wherein

(i) said population of nucleic acid molecules comprises genomic DNA or RNA molecules,

(ii) one strand of said polynucleotide molecule includes-comprises a target nucleic acid sequence and a distinguishing element,

(iii) said target nucleic acid sequence is within 100 nucleotides of said a-distinguishing element in said one strand of said polynucleotide molecule, and

(iv) said distinguishing element distinguishes said polynucleotide molecule from another genomic DNA or RNA molecule that is nearly identical to said polynucleotide molecule;

(b) contacting said population of nucleic acid molecules with a targeting element containing a covalently attached separation group, wherein said targeting element-separation group binds specifically to said target nucleic acid sequence in said polynucleotide molecule;

(c) selectively stabilizing the binding of said targeting element-separation group to said target nucleic acid sequence, wherein stabilization of said targeting element-separation group occurs only if said targeting element-separation group is bound to said target nucleic acid sequence, and said distinguishing element is present within 100 nucleotides of the location to which said bound targeting element binds;

(d) immobilizing said stabilized targeting element via said attached separation group to a substrate, thereby forming an immobilized targeting element-separation group complex comprising the polynucleotide molecule of step (a); and

(e) removing said immobilized targeting element-separation group complex comprising the polynucleotide molecule of step (a) from said population of nucleic acid molecules, wherein said polynucleotide molecule remains bound to said immobilized targeting

element-separation group following said removal, thereby separating said polynucleotide molecule from said population of nucleic acid molecules.

51. (Previously Presented) The method of claim 50, where the targeting element is an oligonucleotide.

52. (Previously Presented) The method of claim 50, where the targeting element binds within 20 nucleotides of said distinguishing element.

53. (Previously Presented) The method of claim 50, where the distinguishing element is a sequence polymorphism.

54. (Previously Presented) The method of claim 50, wherein the polymorphism is a single nucleotide polymorphism.

55. (Previously Presented) The method of claim 50, where the targeting element-separation group is an oligonucleotide comprising a biotinylated nucleotide.

56. (New) The method of claim 1 wherein said population of nucleic acid molecules is a population of genomic DNA molecules, said first targeting element is an oligonucleotide, and said first distinguishing element is a single nucleotide polymorphism.

57. (New) The method of claim 56, wherein said first target nucleic acid sequence is immediately next to said first distinguishing element, said first separation group comprises a terminating nucleotide complementary to said single nucleotide polymorphism and an immobilizable group, and said first separation group is attached to said first targeting element by extending said oligonucleotide in the presence of said first separation group.

58. (New) The method of claim 56, wherein the 3' terminus of said oligonucleotide is complementary to said single nucleotide polymorphism.

59. (New) The method of claim 58 wherein said first separation group comprises a non-terminating nucleotide and an immobilizable group, and said first separation group is attached to said first targeting element by extending said oligonucleotide in the presence of said first separation group.

60. (New) The method of claim 40 wherein said separation group is a modified, non-terminating nucleotide.

61. (New) The method of claim 40 wherein said separation group comprises a fluorescein-modified nucleotide, and said substrate comprises beads coated with antibodies that specifically bind to said fluorescein-modified nucleotide.

62. (New) The method of claim 40 wherein said separation group comprises a cleavable linker.

63. (New) The method of claim 40 wherein said targeting element comprises a cleavable linker.

64. (New) The method of claim 60 wherein said separation group is attached to said targeting element by extending said oligonucleotide in the presence of said modified, non-terminating nucleotide to form an extension product.

65. (New) The method of claim 64 wherein said extension product comprises multiple separation groups.

66. (New) The method of claim 65 wherein said extension product is immobilized to said substrate via said multiple separation groups.

67. (New) The method of claim 66 wherein said polynucleotide molecule is topologically attached to said substrate via said extension product.

68. (New) The method of claim 60 wherein said substrate is a streptavidin-coated surface, said modified, non-terminating nucleotide is a biotinylated nucleotide, and extending said oligonucleotide in the presence of said modified, non-terminating nucleotide topologically links said polynucleotide molecule to said substrate.

69. (New) The method of claim 67 further comprising washing said polynucleotide molecule topologically attached to said substrate at high stringency.

70. (New) The method of claim 39 wherein step (d) is performed with relative motion between said bound oligonucleotide and said substrate to achieve selectivity and efficiency in forming said immobilized oligonucleotide-separation group complex.

71. (New) The method of claim 39, wherein said population of nucleic acid molecules is a population of genomic DNA molecules, and wherein prior to step (b), said genomic DNA molecules are denatured.

72. (New) The method of claim 71, wherein said genomic DNA molecules are denatured with NaOH or by heat.

73. (New) The method of claim 39, wherein said population of nucleic acid molecules is a population of genomic DNA molecules, and said oligonucleotide is coated with a DNA-binding protein to facilitate the binding of said oligonucleotide to said target nucleic acid sequence in said one strand of said polynucleotide molecule.

74. (New) The method of claim 73, wherein said DNA-binding protein is RecA.

75. (New) The method of claim 39 further comprising (f) characterizing said polynucleotide molecule separated from said population of nucleic acid molecules.

76. (New) The method of claim 75 wherein said population of nucleic acid molecules is a population of genomic DNA molecules, and wherein step (f) comprises characterizing sites constituting a haplotype.

77. (New) The method of claim 43, wherein said nucleic acid sequence of interest is a plasmid DNA molecule.

78. (New) The method of claim 50 wherein said population of nucleic acid molecules is a population of genomic DNA molecule, said targeting element is an oligonucleotide, and said distinguishing element is a single nucleotide polymorphism.

79. (New) The method of claim 78 wherein the 3' terminus of said oligonucleotide is complementary to said single nucleotide polymorphism.

80. (New) The method of claim 79 wherein said separation group comprises a non-terminating nucleotide and an immobilizable group, and said separation group is attached to said targeting element by extending said oligonucleotide in the presence of said separation group.

81. (New) The method of claim 50 wherein said separation group is a modified, non-terminating nucleotide.

82. (New) The method of claim 50 wherein said separation group comprises a fluorescein-modified nucleotide, and said substrate comprises beads coated with antibodies that specifically bind said fluorescein-modified nucleotide.

83. (New) The method of claim 50 wherein said separation group comprises a cleavable linker.

84. (New) The method of claim 50 wherein said targeting element comprises a cleavable linker.

85. (New) The method of claim 81 wherein said targeting element is an oligonucleotide, and wherein said separation group is attached to said targeting element by extending said oligonucleotide in the presence of said modified, non-terminating nucleotide to form an extension product.

86. (New) The method of claim 85 wherein said extension product comprises multiple separation groups.

87. (New) The method of claim 86 wherein said extension product is immobilized to said substrate via said multiple separation groups.

88. (New) The method of claim 87 wherein said polynucleotide molecule is topologically attached to said substrate via said extension product.

89. (New) The method of claim 81 wherein said substrate is a streptavidin-coated surface, said targeting element is an oligonucleotide, said modified, non-terminating nucleotide is a biotinylated nucleotide, and extending said oligonucleotide in the presence of said modified, non-terminating nucleotide topologically links said polynucleotide molecule to said substrate.

90. (New) The method of claim 88 further comprising washing said polynucleotide molecule topologically attached to said substrate at high stringency.

91. (New) The method of claim 50 wherein step (d) is performed with relative motion between said stabilized target element-separation group of step (c) and said substrate to achieve selectivity and efficiency in forming said immobilized oligonucleotide-separation group complex comprising the polynucleotide molecule of step (a).

92. (New) The method of claim 50, wherein said population of nucleic acid molecules is a population of genomic DNA molecules, and wherein prior to step (b), said genomic DNA molecules are denatured.

93. (New) The method of claim 92, wherein said genomic DNA molecules are denatured with NaOH or by heat.

94. (New) The method of claim 50, wherein said population of nucleic acid molecules is genomic DNA molecules, and said oligonucleotide is coated with a DNA-binding protein to facilitate the binding of said oligonucleotide to said target nucleic acid sequence of said polynucleotide molecule.

95. (New) The method of claim 94, wherein said DNA-binding protein is RecA.

96. (New) The method of claim 50 further comprising (f) characterizing said polynucleotide molecule separated from said population of nucleic acid molecules.

97. (New) The method of claim 96 wherein said population of nucleic acid molecules is genomic DNA molecules, and wherein step (f) comprises characterizing sites constituting a haplotype.

98. (New) The method of claim 39 wherein steps (a) to (e) are performed in an automated high-throughput format.

99. (New) The method of claim 39 wherein steps (a) to (e) are performed in a miniaturized and integrated format.

100. (New) The method of claim 50 wherein steps (a) to (e) are performed in an automated high-throughput format.

101. (New) The method of claim 50 wherein steps (a) to (e) are performed in a miniaturized and integrated format.